Gene expression profiling of NF-1-associated and sporadic pilocytic astrocytoma identifies aldehyde dehydrogenase 1 family member L1 (ALDH1L1) as an underexpressed candidate biomarker in aggressive subtypes.


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Pilocytic astrocytomas (PAs) are World Health Organization Grade I gliomas; they most often affect children and young adults and occur in patients with neurofibromatosis type 1 (NF1). To identify genes that are differentially expressed in sporadic (S-PA) versus NF1-associated PAs (NF1-PAs) and those that might reflect differences in clinical behavior, we performed gene expression profiling using Affymetrix U133 Plus2.0 GeneChip arrays in 36 S-PAs and 11 NF1-PAs. Thirteen genes were overexpressed, and another 13 genes were underexpressed in NF1-PAs relative to S-PAs. Immunohistochemical studies performed on 103 tumors, representing 2 independently generated tissue microarrays, confirmed the differential expression of CUGBP2 (p = 0.0014), RANBP9 (p = 0.0075), ITGAV1 (p = 0.0001), and INFGR1 (p = 0.024) proteins. One of the underexpressed genes, aldehyde dehydrogenase 1 family member L1 (ALDH1L1), was also reduced in clinically aggressive compared with typical PAs (p = 0.01) and in PAs with increased cellularity and necrosis. Furthermore, in an additional independent set of tumors, weak to absent ALDH1L1 expression was found in 13 (72%) of 18 clinically aggressive PAs, in 8 (89%) of 9 PAs with pilomyxoid features, in 7 (70%) of 10 PAs with anaplastic transformation, and in 16 (76%) of 21 diffusely infiltrating astrocytomas of various grades. In summary, we have identified a molecular signature that distinguishes NF1-PA from S-PA and found that ALDH1L1 underexpression is associated with aggressive histology and/or biologic behavior.

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